

AMENDMENTS TO CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application.

1.-32. (cancelled)

33. (currently amended) A method of inhibiting expression of human HIF-1 alpha mRNA comprising administering to a subject an effective amount of an siRNA comprising a sense RNA strand and an antisense RNA strand, wherein the sense and an antisense RNA strands form an RNA duplex, and wherein the sense RNA strand comprises a nucleotide sequence substantially identical to a target sequence of about 19 to about 25 contiguous nucleotides in human HIF-1 alpha mRNA such that human HIF-1 alpha mRNA is degraded and wherein said target sequence is SEQ ID NO. 223.

34. (original) The method of claim 33, wherein the subject is a human being.

35. (previously presented) The method of claim 33, wherein expression of human HIF-1 alpha mRNA is inhibited in one or both eyes of the subject.

36. (previously presented) The method of claim 33, wherein expression of human HIF-1 alpha mRNA is inhibited in retinal pigment epithelial cells of the subject.

37. (previously presented) The method of claim 33, wherein the effective amount of the siRNA is an amount which provides an intercellular concentration at or near a neovascularization site of from about 1 nM to about 100 nM.

38. (original) The method of claim 33, wherein the siRNA is administered in conjunction with a delivery reagent.

39. (original) The method of claim 38, wherein the delivery agent is selected from the group consisting of lipofectin, lipofectamine, cellfectin, polycations, and liposomes.

40. (cancelled)

41. (previously presented) The method of claim 33, wherein the siRNA is delivered at or near a site of angiogenesis.

42.-45. (cancelled)

46. (withdrawn) The method of claim 33, wherein the siRNA is expressed from a recombinant plasmid

47. (original) The method of claim 33, wherein the siRNA is expressed from a recombinant viral vector.

48. (original) The method of claim 47, wherein the recombinant viral vector comprises an adenoviral vector, an adeno-associated viral vector, a lentiviral vector, a retroviral vector, or a herpes virus vector.

49. (previously presented) The method of claim 48, wherein the recombinant viral vector is pseudotyped with vesicular stomatitis virus, rabies virus, Ebola virus, or Mokola virus.

50. (original) The method of claim 47, wherein the recombinant viral vector comprises an adeno-associated viral vector.

51. (withdrawn) The method of claim 33, wherein the siRNA is administered by an enteral administration route.

52. (withdrawn) The method of claim 51, wherein the enteral administration route is selected from the group consisting of oral, rectal, and intranasal.

53. (original) The method of claim 33, wherein the siRNA is administered by a parenteral administration route.

54. (original) The method of claim 53, wherein the parenteral administration route is selected from the group consisting of intravascular administration, peri- and intra-tissue administration, subcutaneous injection or deposition, subcutaneous infusion, intraocular administration, and direct application at or near the site of neovascularization.

55. (withdrawn) The method of claim 54, wherein the intravascular administration is selected from the group consisting of intravenous bolus injection, intravenous infusion, intra-arterial bolus injection, intra-arterial infusion and catheter instillation into the vasculature.

56. (withdrawn) The method of claim 54, wherein the peri- and intra-tissue injection comprises peri-tumoral injection or intra-tumoral injection.

57. (original) The method of claim 54, wherein the intraocular administration comprises intravitreal, intraretinal, subretinal, subtenon, peri- and retro-orbital, trans-corneal or trans-scleral administration.

58. (withdrawn) The method of claim 54, wherein the direct application at or near the site of neovascularization comprises application by catheter, corneal pellet, eye dropper, suppository, an implant comprising a porous material, an implant comprising a non-porous material, or an implant comprising a gelatinous material.

59. (withdrawn) The method of claim 54, wherein the site of neovascularization is in the eye, and the direct application at or near the site of neovascularization comprises application by an ocular implant.

60. (withdrawn) The method of claim 59, wherein the ocular implant is biodegradable.

61. (currently amended) A method of inhibiting angiogenesis in a subject, comprising:

administering to a subject an effective amount of an siRNA comprising a sense RNA strand and an antisense RNA strand, wherein the sense and an antisense RNA strands form an RNA duplex, and wherein the sense RNA strand comprises a nucleotide sequence substantially identical to a target sequence of about 19 to about 25 contiguous nucleotides in human HIF-1 alpha mRNA; and

degrading the HIF-1 alpha mRNA in the subject, and wherein said target sequence is SEQ ID NO. 223.

62. (previously presented) The method of claim 61, wherein the angiogenesis is characteristic of a disease.

63. (cancelled)

64. (withdrawn) The method of claim 63, wherein the non-pathogenic angiogenesis is associated with production of fatty tissues or cholesterol production.

65. (withdrawn) The method of claim 63, wherein the non-pathogenic angiogenesis comprises endometrial neovascularization.

66. (original) The method of claim 61, wherein the angiogenesis is inhibited in one or both eyes of the subject.

67. (currently amended) A method of treating an angiogenic disease in a subject, comprising:

administering to a subject an effective amount of an siRNA comprising a sense RNA strand and an antisense RNA strand, wherein the sense and an antisense RNA strands form an RNA duplex, and wherein the sense RNA strand comprises a nucleotide sequence substantially identical to a target sequence of about 19 to about 25 contiguous nucleotides in human HIF-1 alpha mRNA; and

degrading the human HIF-1 alpha mRNA such that angiogenesis associated with the angiogenic disease is inhibited, and wherein said target sequence is SEQ ID NO. 223.

68. (withdrawn) The method of claim 67, wherein the angiogenic disease comprises a tumor associated with a cancer.

69. (withdrawn) The method of claim 68, wherein the cancer is selected from the group consisting of breast cancer, lung cancer, head and neck cancer, brain cancer, abdominal cancer, colon cancer, colorectal cancer, esophagus cancer, gastrointestinal cancer, glioma, liver cancer, tongue cancer, neuroblastoma, osteosarcoma, ovarian cancer, pancreatic cancer, prostate cancer, retinoblastoma, Wilm's tumor, multiple myeloma, skin cancer, lymphoma, and blood cancer.

70. (original) The method of claim 67, wherein the angiogenic disease is selected from the group consisting of diabetic retinopathy, age-related macular degeneration, and inflammatory diseases.

71. (withdrawn) The method of claim 70, wherein the inflammatory disease is psoriasis or rheumatoid arthritis.

72. (original) The method of claim 70, wherein the angiogenic disease is age-related macular degeneration.

73. (original) The method of claim 67, wherein the siRNA is administered in combination with a pharmaceutical agent for treating the angiogenic disease, which pharmaceutical agent is different from the siRNA.

74. (withdrawn) The method of claim 73, wherein the angiogenic disease is cancer, and the pharmaceutical agent comprises a chemotherapeutic agent.

75. (previously presented) The method of claim 73, wherein the pharmaceutical agent is selected from the group consisting of cisplatin, carboplatin, cyclophosphamide, 5-fluorouracil, adriamycin, daunorubicin, and tamoxifen.

76. (original) The method of claim 67, wherein the siRNA is administered to a subject in combination with another therapeutic method designed to treat the angiogenic disease.

77. (withdrawn) The method of claim 76, wherein the angiogenic disease is cancer, and the siRNA is administered in combination with radiation therapy, chemotherapy or surgery.